

Viral Hepatitis

Educational objectives:

◊ outline the epidemiology of viral hepatitis whether it's a very big problem or a small problem including the economic verging of this disease group of diseases.

◊ list the cause of viral hepatitis to state this clearly when we talk about viral hepatitis by this we mean those viruses with specific predilection to selectively affect the liver , A, B, C, D, and E they set to be hepatotropic means they like the liver, there are other viruses though that cause hepatitis but they infect any organ system such as : adenovirus, cytomegalovirus, EBV, these can cause hepatitis but they aren't specific for the liver so our talk will be limited to those viruses that selectively infect the liver.

◊ for dentistry you should be able to identify the manifestations of both acute and chronic viral hepatitis so when a patient sets on the chair when you take a problem focused history if (s)he mentions anything suggested about chronic or acute viral hepatitis you should be aware and behave accordingly, this is the most important properly because at the end of the day if we want to diagnose viral hepatitis the symptoms aren't enough simply because they aren't specific we say in medicine they aren't "pathognomonic" there is nothing characteristic or exclusive of viral hepatitis and therefore the diagnosis is difficult based on clinical plan only, that's why we use serology which is laboratory investigations of blood sample to diagnose accurately chronic or acute viral hepatitis.

◊ now this is important as well we should be able to identify those people who are candidates for vaccination you're certainly once, so if anyone isn't vaccinated you should get vaccinated particularly B virus there is low vaccine for C and the vaccine for A is restricted to very limited group of individuals, again if you aren't vaccinated you should manage to be vaccinated as soon as possible.

You might ask why bother you with viral hepatitis? There are several reasons:

First but not last you can get it, if you treat a patient with HBV which is highly infectious it's the worst among all viruses it's worst than C worst than HIV either, as endoscopist when I get a patient with HIV I do the usual precautions nothing super nothing exceptional but if I get patient is HBV infected I get double gloves, mask, goggles, and everything because I know (s)he can infect me 300-500 times more than patients with HIV this why we should be vaccinated.

Now on the other hand you as future dentists can involuntary transmit the virus to the patient simply if you don't sterilize properly your instruments and last but not least patients with dental problems and with chronic liver disease undetected liver disease they can lead to troubles, if you do a procedure on them not knowing their chronic viral illness like if the patient has liver cirrhosis (s)he might have coagulopathy, platelets might be low imagine yourself extracting a tooth for a patient with platelets of 20 (s)he will bleed to death no way to stop that bleeding, so for all these reasons I thought it's important for you to get an idea about what it is viral hepatitis.

Now these are the viruses that we talked about earlier A, B, C, D, and E from the table what you need to know is:

A and E they're similar they are both RNA viruses transmitted by fecal oral route unlike B, C, D which are transmitted parentally (blood, semen,

saliva, etc) they share similar characteristics, remember that viruses A and E they never become chronic that means you can get the acute infection you clear it or you die but don't get chronically, while B, C, and D chronicity is very high especially with C.

Clinical manifestations of acute hepatitis:

First of all you should know among viral hepatitis, A hepatitis is the most likely when acutely infected patients to have symptoms while the least likely to get symptoms with acute infection is C.

As mnemonic from A to C most symptomatic is A least symptomatic is C, in acute infections most of the time all we get in my clinic a patient has had a laboratory check with positive results or people traveling to KSA for instance you should check for hepatitis B they are asymptomatic because acute infection with B and C are asymptomatic.

HEV is most dangerous in pregnant women for some reason mortality rate reaches up to 30% while mortality rate from acute infections with other hepatitis in general B, C, or A 1 out 1000.

HBV can present with no specific symptoms there is nothing like acute myocardial infarction which has specific symptoms like chest pain, here there is nothing specific not even jaundice some of the acute or chronic hepatitis never present with jaundice, many of you might think hepatitis means jaundice this isn't true some 40% of people infected acutely don't have jaundice even 70% with B, C or even 80% they won't develop jaundice so the message is the absence of jaundice doesn't rule out acute hepatitis.

No specific symptoms like fever, arthritis, urticaria, angioedema, it's called serum sickness like picture like someone takes a drug and the drug has some reactions on the patient.

Generally with all acute hepatitis the symptoms improve after appearance of jaundice once the patient get jaundiced (icteric) the patient symptoms of abdominal pain, headache, diarrhea, etc, will become low.

Nothing specific of viral hepatitis.

◊The laboratory tests:

When you get acute viral hepatitis the injury is set to be hepatocellular means the cells swell and they explode and will be leak in the enzymes and they end up in the circulation and when we check the serum we'll find them elevated in general elevation of liver enzymes is more than 10 fold of the upper limit of normal meaning if the upper limit of normal is 30 to have acute hepatitis it should be above 300 but if it 100-150 it will be chronic or resolving you checked the patient in resolving phase.

There are other causes of massive elevation of liver enzymes such as:

- Drug induced like paracetamol for instance or any other drugs can cause it.
- ischemic
- Other viruses.

◊Modest elevations could be:

- Chronic hepatitis
- Metastatic disease to the liver someone has colon cancer it can metastasize to liver and elevate the enzymes and it can also elevate alkaline phosphatase and Bilirubin.
- Biliary obstruction, stone anything compressing on bile duct.
- Acute alcoholic hepatitis someone drinks a whisky bottle it can cause acute hepatitis.

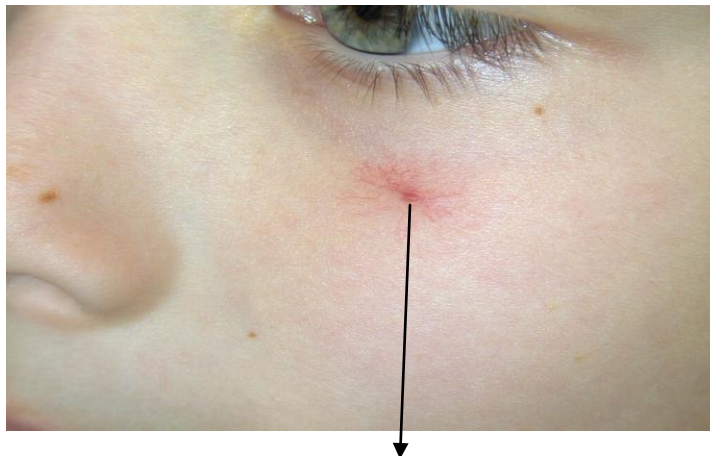
◊Bilirubin and alkaline phosphatase may or may not be elevated the liver enzymes are the most to be elevated.

◊WBC count in general is decreased so the patient will be leucopenic that make sense as you know all viral infections cause leucopenia unlike bacteria which cause leucocytosis.

That was the acute picture what about the chronic picture?

Most of the time patients are completely totally asymptomatic as I mentioned earlier you find during laboratory investigations elevated liver enzymes, viral particles in terms of physical exam on the other hand you can find one of the following:

- Spider agiomata: This is a dilated blood vessel anteriorly posteriorly and from the nipples above.
- Palmar erythema.
- Clubbing of fingers: the nails get clubbed, the normal angle will be less than 180 but here it's more.
- Dupuytren contractures: the fingers bend towards the palm and cannot be fully extended, so they can't close their hands.
- Gynecomastia in males or breast atrophy in females and testicular atrophy as well that's because males get feminized and females get masculinized because of hormones are metabolized in the liver.



This is spider agiomatas: low pit raised at the center if you press on it it'll disappear unlike the vasculitic lesions that contain vasculitis those lesions won't disappear when you press on them.



Palmar erythema: it isn't pathognomonic of liver disease because there are many causes of palmar erythema like: thyrotoxicosis, steroid treatment, pregnancy, etc

This is the normal angle less than 180.



Normal angle of nail bed



Distorted angle of nail bed

Clubbed fingers



ADAM

If you want to diagnose it you ask the patient to place fingernails of same finger on opposite hands against each other, nail to nail and you will see the normal diamond space between fingers if you don't see it this is clubbing of the fingers.

Now we are up to the specific hepatitis we'll talk about them one by one A through E:

Hepatitis A: you just need to know that the incubation period which is the time elapsing between the entry to the body and the first manifestations of the disease it goes between 2-4 weeks it's much longer for B and C, just remember it's weeks not days.

This is important the younger you are the less likely to have symptoms of the infection, the older you are the more likely to have symptoms like jaundice why?

The reason that the virus isn't cytopathic doesn't kill the cells by itself the one who kills is the natural killer cells which are part of the immune system recognize the viral infected cells and eat them up and cause the disease, this is logic because smaller kids they have immature immune system and that's why they don't have much damage to the viral infected cells but in older ages they have mature immune system and thus they are more symptomatic.

◊Complications of hepatitis A:

- You can get fulminant hepatitis and the death is 1 out 1000.
- Prolonged cholestasis you will have jaundice for 6 months but this isn't chronicity because A never becomes chronic.

The serological profile of HAV you just need to know if you want to diagnose acute hepatitis A ask for IgM anti HAV.

The epidemiology as I mentioned you can see it goes with low hygiene standards the water is contaminated, the vegetables etc...

The vaccination for hepatitis A just for selected patients like travelers, food handlers it isn't important.

Now up to the most important virus simply because 8% of you have hepatitis surface antigen believe me out of 100 4-8% they are chronically infected or carriers of hepatitis B, in my clinic I have many students from medicine, dentistry, pharma, etc they don't know that they have it that's the sad picture in Jordan in other countries it's much higher.

The incubation period much longer, clinical illness similar to A as the patients are older they are more prone to get acutely infected, and the younger the lower to get acutely infected.

The exact opposite for chronic illnesses; the younger you are the higher the possibility to get chronic infection because of the immature immune system.

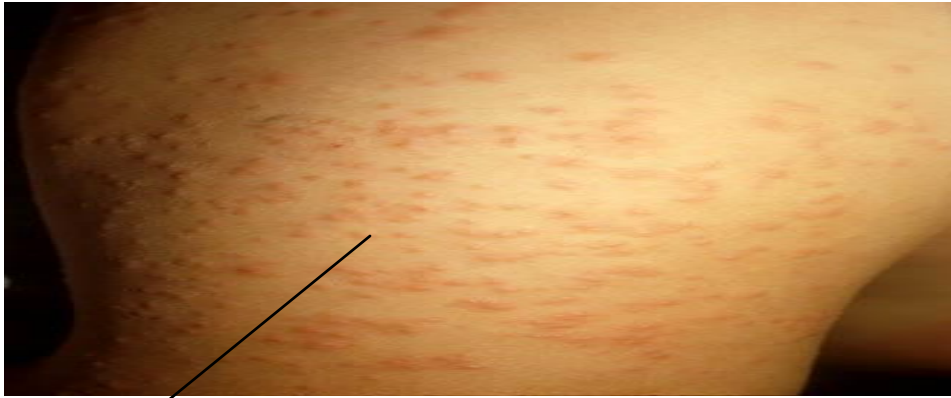
We get extrahepatic manifestations in acute infections such as:

- Arthralgias.
- Papular acrodermatitis.

In chronic infection:

- Glomerulonephritis.
- Arthralgias.
- Polyarteritis nodosa (PAN) which is inflammation of vessels.

These called extrahepatic manifestations and they all so-called the immune complexes because of the immune process.



Papular acrodermatitis this is very rare I saw it 3 times in my life because it doesn't last for long period.

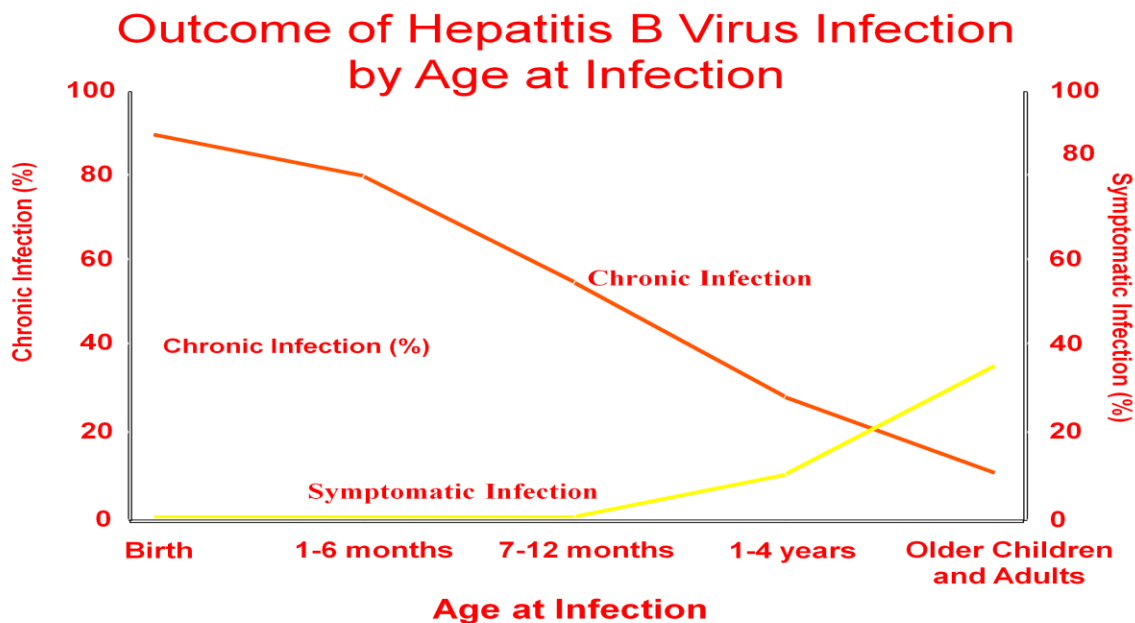


The importance of this if you see a patient has it and you are unable to determine the cause check the serology for hepatitis B most of the time they will be positive.

Hepatitis B isn't the only one has extrahepatic manifestations C also can do that but A and E don't do that because they generally don't get chronic.

Serology for hepatitis B is more complicated remember the first that appear in the blood are the viral particles (DNA) and hepatic surface antigen, the last one to appear in recovery period is the antibody to hepatic surface antigen which is anti HBs.

The acute infection we diagnose it by IgM anti HBc(c=core) if you don't recover remember E antigen still appears but it stops and the antibody will appear so forever will have surface antigen.



The above slide summarizes the concept of young vs. above and acute vs. chronic, note the acute infections which are symptomatic infections the older you are the more likely to get chronic infections the exact opposite the older you are the less likelihood of chronicity.

KSA the highest country with hepatitis B, Egypt about 22% are infected.

B virus can present in all body fluids even in saliva so when working with patient's mouth always be aware to wear double gloves because B is horrible it can survive on dry surfaces if we put it on a table it can survive.

Transmission is parental of course exchange of blood, sexually, vertical mother to baby that's why mandatory to screen all pregnant women for hepatitis B because if the mother is infected the baby should receive as soon as possible both the vaccine and immunoglobulin at several sites at birth.

The diagnosis is relatively easy when we suspect cell surface antigen and get the antibody means there is something in the past, IgM for acute infection, IgG for past or chronic infection, E antigen means infectivity the replication and anti E means are immune so the antigen is pad and the antibody is good, the DNA we use it for monitoring the effectiveness of therapy.

I may ask you a question like: a patient has surface antigen positive, antibody for B is positive, surface antibody is negative (s)he has one of 3:

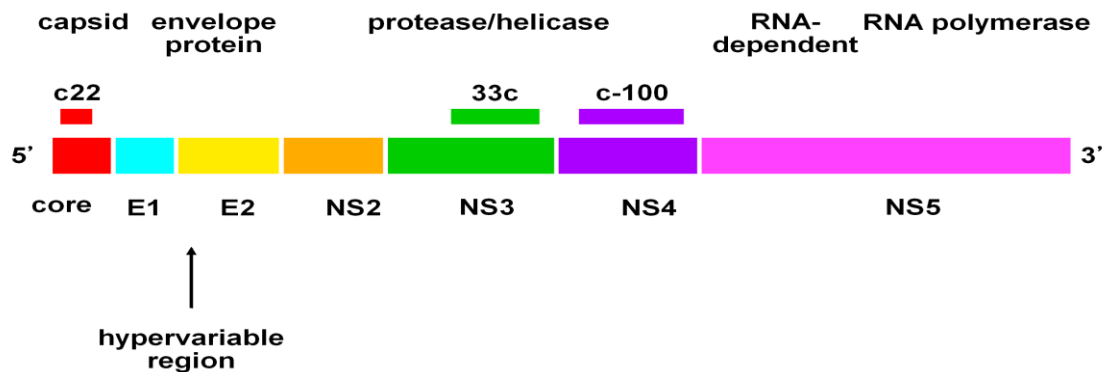
- **Acutely infected.**
- **Chronically infected with elevated liver enzymes.**
- **Carrier if liver enzymes are normal.**

We have many scenarios based on serology you will decide if the patient is acutely infected, immunized, etc...

You might find everything is negative no surface antigen no core antibody but there are only antibodies for surface antigen that means the patient has been immunized the vaccine is working.

So vaccination this is the best way to go.

Hepatitis C: this is secondly importance to hepatitis B, 400 million people are infected with B they have surface antigen, over 2 billion people have remote infection no other infections like B, 1/3 of the world population are at some point infected with B 1/5 of these remain chronically carriers of surface antigens of B while C it's about 179 million are infected and 59 million for AIDS, so B ranking 1 for chronic infection.



The above is the structure of C, there are different genotypes 1 through 6, there is something called hypervariable region the importance of this that is impossible to make a vaccine it continuously changes itself.

The NS which is nonstructural it's important because currently many of newer medications are developed against.

Basically similarly with B the incubation period is weeks not days, clinical illness rare acute infection 20% of the time will get acute hepatitis C, chronicity is very high more than B definitely, 70-80% of the time you will remain chronically infected.

C unlike B, E, and A it doesn't confer immunity it isn't immunogenic, it will infect you over and over not only one time because it doesn't leave immunity.

Similarly with B you can get extrahepatic manifestations such as:

- Vasculitis.
- Arthritis.
- Glomerulonephritis.

In addition you can get some skin diseases like:

- Porphyria cutanea: which are painful, blistering, itchy lesions.
- Sjogren like syndrome: so they will have xerostomia no saliva.

The serology is anti hepatitis C virus or anti HCV RNA.

◊Risk factors to get C virus basically similarness with B with the exception C is much less likely to be sexually transmitted while B is very high and the following are the risk factors:

- Transfusion or transplant from infected donor
- Injecting drug use
- Hemodialysis (yrs on treatment)
- Accidental injuries with needles/sharps
- Sexual/household exposure to anti-HCV-positive contact
- Multiple sex partners
- Birth to HCV-infected mother

Egypt the highest and I think Mongolia and KSA are on the way to beat Egypt.

HCV positive much less in Jordan actually less than USA.

Laboratory diagnosis:

HCV RNA tells you that there is Proliferation the viral infection is active; antibody alone tells if you are infected, but if you are chronic or got away with nothing that would be answered with HCV RNA level if you have it you are chronically infected even if the enzymes are low.

Prevention:

There is no vaccine just be careful make sure to sterilize, and protect yourself.

Hepatitis D:

It comes with B full package if there is no hepatitis B no D, it's within the envelope of B.

It can coinfect or superinfect, it can become chronic similar with B which makes the picture of B much worse including cancerogenicity.

Hepatitis E:

Affects most commonly pregnant women, in Mexico, the Indian subcontinent, KSA, it most dangerous in pregnant women.

IgM anti hepatitis E it isn't available worldwide; in USA if you want to diagnose it you should send a sample to central disease control (CDC) in Atlanta Georgia.

◊The following table summarizes everything, forget about C and D.

Organism	Acute	Chronic	Recovered/latent	Vaccinated
HAV	<ul style="list-style-type: none"> • Anti-HAV IgM 	<ul style="list-style-type: none"> • NA 	<ul style="list-style-type: none"> • Anti-HAV IgG 	<ul style="list-style-type: none"> • Anti-HAV IgG
HBV	<ul style="list-style-type: none"> • Anti-HBc IgM • HBeAG • HBV DNA 	<ul style="list-style-type: none"> • Anti-HBc IgG • HBsAg • HBeAg or HBeAb 	<ul style="list-style-type: none"> • Anti-HBc IgG • Anti-HBs 	<ul style="list-style-type: none"> • Anti-HBs

Summary:

- Only HBV, HDV and HCV can cause chronic liver disease.
- Accurate diagnosis of viral hepatitis depends on proper interpretation of specific serologic tests.
- Initial management of acute hepatitis is supportive, with monitoring for signs of liver failure.
- Antiviral therapy is effective in selected patients with chronic HCV or HBV.
- Immune globulins and vaccine are given to selected contacts of the patient with acute hepatitis A or B.

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